AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [00023] on page 6 with the following rewritten paragraph:

[00023] In yet another embodiment, ~~ECGC~~ EGCG analogs are provided wherein the analogs contain at least one modification relative to ~~ECGC~~ EGCG *per se* ~~that~~ which results in an IC_{50} of less than 60 when the analogs are evaluated for their ability to inhibit growth in a breast cancer cell line using the MTT assay ~~, using~~ according to the protocol provided by the manufacturer (Promega, Madison, WI).

Please replace paragraph [00034] on page 7 with the following rewritten paragraph:

[00034] As used in the specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a substituent" includes a single substituent as well as two or more substituents that may be the same or different, reference to "a compound" encompasses a combination or mixture of different compounds as well as a single compound, reference to "a pharmaceutically acceptable carrier" includes two or more such carriers as well as a single carrier, and the like.

Please delete paragraph [00035] on page 7.

Please replace paragraph [00062] on page 13 with the following rewritten paragraph:

[00062] R^1, R^2, and R^3 are selected from: hydrogen; hydroxyl; alkyl, preferably C_1-C_6, alkyl, particularly methyl; sulfhydryl; halo; alkoxy, preferably C_1-C_6 alkoxy, such as methoxy and ethoxy, with methoxy preferred; and aryloxy, preferably C_5-C_{12} aryloxy, with phenoxy preferred. The alkoxy [[,]] and aryloxy [[,]] substituents are optionally heteroatom-containing and/or may be substituted with one or more, typically one or two substituents. Of course, it will be appreciated that any substituents should not be detrimental to the therapeutic efficacy of the compound, nor should they be reactive with or otherwise interact adversely with other components of the pharmaceutical composition in which the compound is contained. Substituents include functional groups, hydrocarbyl groups, and combinations thereof as described in part (I) of this section.

Please replace paragraph [00070] n page 15 with the following rewritten paragraph:

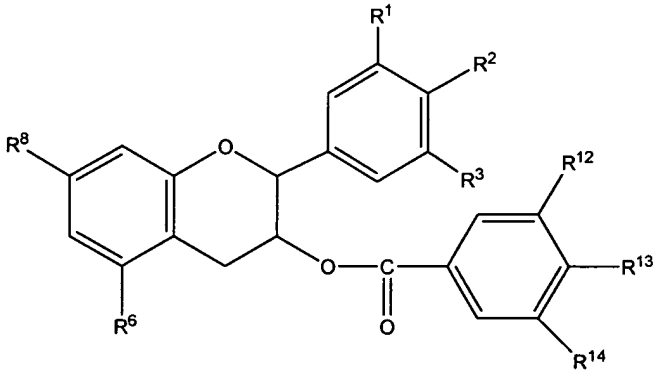
[00070] The aforementioned substituents are defined as indicated with the proviso that the compound of formula (I) excludes the natural products EGCG, EGC, and EC ~~*per se*~~, as well as the 3,4,5-trimethoxybenzoyloxy analog of EGCG, such that when (a) R^7, R^9, R^{10}, and R^{11} are hydrogen, (b) R^1, R^2, R^6, and R^8 are hydroxyl, (c) R^3 is hydrogen or hydroxyl, and (d) R^4 is O, then (e) R^5 is other than 3,4,5-trihydroxybenzoyloxy or 3,4,5-trimethoxybenzoyloxy.

Please replace paragraphs [00075], [00076], and [00077] on pages 17-18 with the following rewritten paragraphs:

[00075] Particularly preferred compounds of formula (I) are wherein: R^4 is O; R^5 is an ester substituent R-(CO)-O- wherein R is phenyl substituted at the 3-, 4-, and 5-positions with substituents independently selected from the group consisting of hydroxyl, methyl, and methoxy; and R^7, ~~and~~ R^9, R^{10}, and R^{11} are hydrogen.

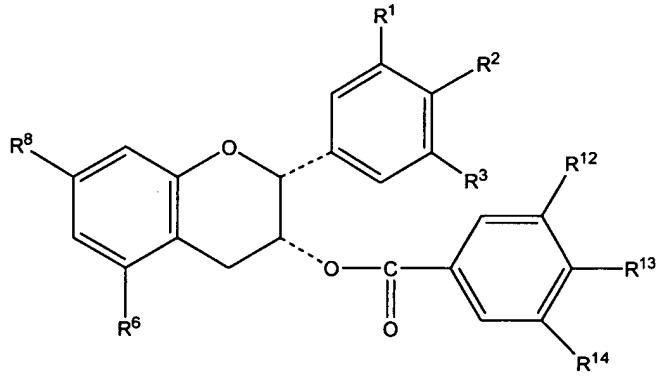
[00076] Accordingly, particularly preferred compounds of the invention have the structure (III)

(III)

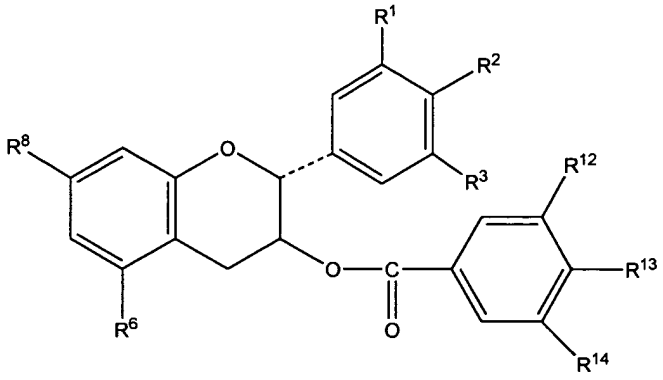


~~having~~ in either the cis (IVA) or trans (IVB) form ~~structures (IVA) and (IVB)~~

(IVA)



(IVB)



[00077] In a most preferred embodiment, R^1, R^2, R^3, R^6, R^8, R^{12}, R^{13}, and R^{14} are independently selected from hydroxyl, methyl, ~~or~~ and methoxy, with the proviso that the compound of formula (I) excludes EGCG *per se*, such that when (i) R^1, R^2, R^6, and R^8 are hydroxyl, and (ii) R^3 is hydroxyl, then (e) R^5 is other than 3,4,5-trihydroxybenzoyloxy or 3,4,5-trimethoxybenzoyloxy.

Please delete paragraph [00078] on page 18.

Please replace paragraph [00081] on page 24 with the following rewritten paragraph:

[00081] R^1, R^2, and R^3 are selected from the group consisting of hydroxyl; alkyl, preferably C_1-C_6 alkyl, particularly C_1-C_6 alkyl, with methyl preferred; halo; sulfhydryl; alkoxy, preferably C_1-C_6 alkoxy, such as methoxy and ethoxy, with methoxy preferred; and aryloxy, preferably C_5-C_{12} aryloxy, with phenoxy preferred. The alkoxy [[,]] and aryloxy [[,]] substituents are optionally heteroatom-containing and/or may be substituted with one or more, typically one or two substituents. As noted above, any substituents should not be detrimental to the therapeutic efficacy of the compound, nor should they be reactive with or otherwise interact adversely with other components of the pharmaceutical composition in which the compound is contained. Substituents include functional groups, hydrocarbyl groups, and combinations thereof as described in part (I) of this section.

Please replace paragraph [00084] on page 25 with the following rewritten paragraph:

[00084] In a further embodiment, ~~ECGC~~ EGCG analogs are provided wherein the analogs contain at least one modification relative to ~~ECGC~~ EGCG *per se* that results in an IC_{50} of less than 60 when using the analogs are evaluated for their ability to inhibit growth in a breast cancer cell line using ~~MTT assay,~~

~~using~~ the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in a protocol provided by the manufacturer (Promega, Madison, WI). Such compounds are useful as precursors for the compounds of formulae (I) and (II), and possibly as therapeutic agents, such as chemotherapeutic and ~~chemopreventative~~ chemopreventive agents.

Please replace paragraph [000126] on page 38 with the following rewritten paragraph:

[000126] (b) Preparation of chalcone **13**: A mixture of 4,6-dibenzyloxy-2-hydroxy-acetophenone **2** (15 g, 0.043 mol) and 3,4,5-tribenzyloxybenzaldehyde **12** (20.1 g, 0.047 mol) in ethanol (400 mL) was placed in a three-necked flask fitted with an overhead stirrer and condenser. Piperidine (80 mL) was then added and the mixture was heated to reflux for 24 h. A yellow solid precipitated out. The reaction mixture was cooled and filtered to afford a yellow solid, which was washed with cold ethanol and dried to afford the chalcone **13** as a yellow solid (60% yield). TLC: methylene chloride: Rf=0.51; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.87 (s, 4H, CH_2OPh), 5.12 (m, 6H, CH_2OPh), 6.18 (d, 1H, 3'-Ar-H), 6.25 (d, 1H, 5'-Ar-H), 6.70 (s, 2H, 2, 6-Ar-H), 7.19-7.45 (m, 25H, OBn-Ar-H), 7.66 (d, 1H, C(O)-CH=CH-), 7.78 (d, 1H, C(O)-CH=CH-), 14.21 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 70.39, 71.20, 75,26, 93.07, 95.22, 108.44, 127.10-128.83, 130.84, 135.80, 135.94, 136.89, 142.46, 152.92, 161.55, 165.24, 168.17, 192.63. Anal. Calcd. for $C_{50}H_{42}O_7$ (754.88): C 79.56, H 5.61; Found: C 79.47, H 5.64.

Please replace paragraph [000134] on page 40 with the following rewritten paragraph:

[000134] (a) Preparation of (2E)-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4,5-tribenzyloxy-phenyl)prop-2-en-1-one (19): To a suspension of NaH (1.63 g, 40.78 mmol, 60% in mineral oil w/w) in 50 mL of freshly distilled DMF, was portion wise added 4,6-dimethyoxy-2-hydroxyacetophenone 18 (5 g, 25.50 mmol) at room temperature. The mixture was left to stir for 1 hour until all H2 evolution was ceased. Tribenzyloxybenzaldehyde 12 (13 g, 30.60 mmol) was then added all at once and the mixture continued to stir for an additional 30 minutes, after which the solution gradually became dark red. The mixture was diluted with water and a yellow solid precipitated from solution. The solid thus obtained was filtered off and washed several times with cold methanol, and dried under reduced pressure (15 mmHg at room temperature) overnight to provide 14.12 g (92% yield) of pure chalcone 19. ~~1H~~ ^{1}H NMR (300 MHz, ~~CDCl3~~ $CDCl_3$): ~~δ~~ δ 3.81 (s, 3H, ~~OCH3~~ OCH_3), 3.84 (s, 3H, ~~OCH3~~ OCH_3), 5.12 (s, 2H, ~~OCH2Ph~~ OCH_2Ph), 5.16 (s, 4H, ~~OCH2Ph~~ OCH_2Ph), 5.94 (d, J=2.7 Hz, 1H, CH=CH), 6.10 (d, J=2.7 Hz, 1H, CH=CH), 6.88 (s, 2H, 2',6'-Ar-H), 7.26-7.44 (m, 17H, Ar-H, 6,8-H), 14.25 (s, 1H, OH). ~~13C~~ ^{13}C NMR (~~CDCl3~~ $CDCl_3$): 55.59, 55.80, 71.34, 75.31, 91.29, 93.83, 106.34, 108.32, 126.87, 127.31, 127.46,

127.94, 127.98, 128.20, 128.58, 131.13, 136.86, 137.55, 140.90, 142.30, 153.02, 162.41, 166.19, 168.34, 192.37.

Please replace paragraphs [000136] to [000139] on pages 40-42 with the following rewritten paragraphs:

[000136] The 3-flavene 20 was synthesized by the same procedure as for the synthesis of 3-flavene 5, (Scheme 1), using ~~NaBH4/THF/EtOH~~ $NaBH_4$/THF/EtOH. 20 was isolated in 52% yield as a white solid after flash chromatography using methylene chloride. ~~1H~~ ^1H NMR (300 MHz, ~~CDCl3~~ $CDCl_3$): ~~δ~~ δ 3.75 (s, 3H, ~~OCH3~~ OCH_3), 3.78 (s, 3H, ~~OCH3~~ OCH_3), 5.02 (s, 2H, ~~OCH2Ph~~ OCH_2Ph, 5.09 (s, 4H, ~~OCH2Ph~~ OCH_2Ph), 5.52 (dd, J=3.6, 9.6 Hz, 1H, 4-H), 5.69-5.72 (m, 1H, 3-H), 6.05 (s, 2H, 2',6'-Ar-H), 6.76 (s, 2H, 6,8-Ar-H), 6.78 (dd, J=1.8, 9.6 Hz, 1H, 2-H), 7.24-7.43 (m, 15H, Ar-H). ~~13C~~ ^{13}C NMR (~~CDCl3~~ $CDCl_3$): 55.61, 55.86, 71.46, 75.43, 77.52, 92.15, 94.01, 104.59, 107.21, 119.20, 119.85, 127.78, 127.97, 128.06, 128.36, 128.66, 128.74, 136.69, 137.29, 138.14, 138.79, 153.15, 155.06, 156.52, 161.53.

[000137] (c) Preparation of (2,3-trans)-5,7-dimethoxy-2-(3,4,5-tribenzyloxyphenyl)chroman-3-ol (21): The flavanol 21 was synthesized by the same hydroboration/oxidation sequence from 20, as used for 6, yielding exclusively the 2,3-trans alcohol 21 as a white solid in 83 % yield after silica gel chromatography, eluting 30% ethyl acetate in hexanes. ~~1H~~ ^1H NMR (300 MHz, CDCl3): ~~δ~~ δ 1.63 (d, J=3.6 Hz, 1H, OH), 2.55 (dd, J=8.7, 16.5 Hz, 1H, 4-H), 2.98 (dd, J=5.7, 16.5 Hz, 1H, 4-H), 3.74 (s, 3H, ~~OCH3~~ OCH_3), 3.78 (s, 3H, ~~OCH3~~ OCH_3), 3.90-4.00 (m, 1H, 3-H), 4.59 (d, J=7.8 Hz, 1H, 2-H), 5.05 (s, 2H, ~~OCH2Ph~~ OCH_2Ph), 5.08 (s, 2H, ~~OCH2Ph~~ OCH_2Ph), 5.09 (s, 2H, ~~OCH2Ph~~ OCH_2Ph), 6.10 (d, J=2.4 Hz, 1H, 8-H), 6.12 (d, J=2.4 Hz, 1H, 6-H), 6.73 (s, 2H, 2',6'-H), 7.22-7.43 (m, 15H, Ar-H). ~~13C~~ ^{13}C NMR (CDCl3) 27.57, 55.61, 55.74, 68.50, 71.49, 75.42, 77.43, 82.04, 92.23, 93.24, 101.78, 107.05, 127.78, 128.05, 128.16, 128.39, 128.71, 128.76, 133.57, 137.09, 138.01, 153.28, 155.30, 159.00, 160.00.

[000138] (d) Preparation of SR 13198: The hexabenzyloxy-protected precursor of SR 13198 was prepared from 21 as follows. A mixture of 21 (400 mg, 0.66 mmol), 3,4,5-tribenzyloxy-benzoic acid (585 mg, 1.32 mmol), EDC (761 mg, 3.97 mmol), 1-hydroxybenzotriazole HOBt (358 mg, 2.65 mmol), DMAP (323 mg, 2.65 mmol), triethylamine (461 ~~L~~ µL, 3.31 mmol) and methylene chloride (15 mL) was stirred at room temperature under argon for 18-24 hours after which all starting alcohol was consumed as confirmed by TLC. The mixture was then poured into 20 mL of 2N HCl solution, extracted with ethyl acetate, dried over magnesium sulfate and evaporated to dryness. The crude thus obtained was purified by flash chromatography on silica gel using 20 % of ethyl acetate in hexanes to afford a white solid (650 mg, 96 % yield). ~~1H~~ ^1H NMR (300 MHz, CDCl3): 2.74 (dd, J=6.6, 17.1 Hz, 1H, 4-H), 2.95 (dd, J=5.7, 17.1 Hz, 1H, 4-H), 3.79 (s, 3H, ~~OCH3~~ OCH_3), 3.81 (s, 3H, ~~OCH3~~ OCH_3), 4.98-5.22 (m, 13H,

~~OCH2Ph~~ OCH_2Ph, 3-H), 5.38-5.44 (m, 1H, 2-H), 6.15 (d, J=1.5 Hz, 8-H), 6.21 (d, J=1.5 Hz, 6-H), 6.71 (s, 2H, 2',6'-H), 7.20-7.45 (m, 32H, Ar-H, 2", 6"-H).

[000139] The hydrogenolysis of this hexabenzyloxy ester as described above for the syntheses of Examples 1-4 gave the desired polyphenol SR 13198 in 86 % yield as a yellowish solid after reverse phase chromatography using a gradient of methanol in water (from 7/3 then 1/1 then 3/7 respectively). ~~1H~~ ^1H NMR (300 MHz, acetone-d6): 2.75-2.79 (m, 2H, 4-H), 3.77 (s, 3H, ~~OCH3~~ OCH_3), 3.78 (s, 3H, ~~OCH3~~ OCH_3), 5.16 (d, J=4.8 Hz, 1H), 5.40 (q, J=4.8 Hz, 1H), 6.13 (d, J=2.4 Hz, 1H, 8-H), 6.15 (d, J=2.4 Hz, 1H, 6-H), 6.46 (s, 2H, 2',6'-H), 7.03 (s, 2H, 2", 6"-H), 7.25 (s, 1H, OH), 7.84 (s, 2H, OH), 7.99 (s, 1H, OH), 8.16 (s, 2H, OH). MS (ESI, negative ion mode) 485 (M-1), 971 (2M-1).

Please replace paragraph [000168] on page 53 with the following rewritten paragraph:

[000168] To establish that the analogs of EGCG also act via the same mechanisms as EGCG itself, the active analog SR 13196 in cell cycle studies in MCF-7 cells was examined. As shown in FIGs 6A to 6C. SR 13196 at 10 ~~□M~~ μM (FIG. 6B), arrests the cell cycle in G1, similar to the effect of 10 μM of EGCG (FIG. 6C) but more pronounced.